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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/588,911	08/09/2006	Susan Elizabeth Bove	PC32145A	8818
26648 7590 01/30/2009 PHARMACIA CORPORATION GLOBAL PATENT DEPARTMENT POST OFFICE BOX 1027 ST. LOUIS, MO 63006			EXAMINER MERTZ, PRIMA MARIA	
			ART UNIT 1646	PAPER NUMBER
			MAIL DATE 01/30/2009	DELIVERY MODE PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

10/588,911

Applicant(s)

BOVE ET AL.

Examiner

Prema M. Mertz

Art Unit

1646

Period for Reply -- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 12 December 2008.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-13 is/are pending in the application.
- 4a) Of the above claim(s) 3-5 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1,2 and 6-13 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-8506)
Paper No(s)/Mail Date 8/9/06
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date _____
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: _____

DETAILED ACTION

Claims 1-13 are pending in the instant application. Claims 1, 13, have been amended in the response filed 12/12/08.

Election/Restriction

1. Applicant's election of Group 2 (claims 1-2, 6-13) in the reply filed on 12/12/08 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claims 3-5 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected claims, there being no allowable generic or linking claim.

Specification

2. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed. It is suggested that the title of the invention be amended to recite a method of treating osteoarthritis by administering an IL-6 antibody.

Claim rejections-35 USC § 101

3. 35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claim 13 is rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. The claim embraces a use of an IL-6 antibody and there are no provisions for "use" in the statutes. Amending the claims to recite "a process or a method" will obviate this rejection, but does not prevent the Examiner from making the next office Action final.

In view of the improper format for claim 13, the claim will be examined for a reasonable interpretation of its intended meaning.

Claim rejections-35 USC § 112, first paragraph

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

- 4a. Claim 8 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The monoclonal antibody from a hybridoma recited in claim 8, is essential to the claimed invention. The reproduction of antibodies from the disclosed hybridomas is an extremely unpredictable event. The antibody from the hybridoma with accession number CNTO 328, must be obtainable by a repeatable method set forth in the specification or otherwise be readily

available to the public. The instant specification does not disclose a repeatable process to obtain the antibody from the hybridoma, and it is not apparent if the hybridoma is readily available to the public. If the deposit has been made under the terms of the Budapest Treaty, an affidavit or declaration by applicants or someone associated with the patent owner who is in a position to make such assurances, or a statement by an attorney of record over his or her signature, stating that the hybridoma has been deposited under the Budapest Treaty and that the hybridoma will be irrevocably and without restriction or condition be released to the public upon the issuance of a patent would satisfy the deposit requirement made herein. See 37 CFR 1.808. Further, the record must be clear that the deposit will be maintained in a public depository for a period of 30 years after the date of deposit or 5 years after the last request for a sample or for the enforceable life of the patent whichever is longer. See 37 CFR 1.806. If the deposit has not been made under the Budapest treaty, then an affidavit or declaration by applicants or someone associated with the patent owner who is in a position to make such assurances, or a statement by an attorney of record over his or her signature must be made, stating that the deposit has been made at an acceptable depository and that the criteria set forth in 37 CFR 1.801-1.809, have been met.

Amendment of the specification to disclose the date of deposit and the complete name and address of the depository is required.

If the deposit was made after the effective filing date of the application for a patent in the United States, a verified statement is required from a person in a position to corroborate that the hybridomas described in the specification as filed are the same as that deposited in the depository. Corroboration may take the form of a showing of a chain of custody from applicant to the depository coupled with corroboration that the deposit is identical to the biological

material described in the specification and in the applicant's possession at the time the application was filed.

Applicant's attention is directed to *In re Lundak*, 773 F.2d. 1216, 227 USPQ 90 (CAFC 1985), and 37 CFR 1.801-1.809 for further information concerning deposit practice.

Claim Rejections - 35 USC § 112, second paragraph

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-2, 6-13, are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1, line 2, is rejected as vague and indefinite because the limitation “a osteoarthritis” is improper. It is unclear what the metes and bounds of the term “a osteoarthritis” is.

Claim 13, lines 2-3, are rejected as vague and indefinite for the recitation of “an anti-IL-6 receptor antibody” which is non-elected subjected matter.

Claims 2, 6-12, are rejected as vague and indefinite insofar as they depend on the above rejected claims for their limitations.

Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

6a. Claims 1-2, 6-7, 9-13, are rejected under 35 U.S.C. § 103 as being unpatentable over Kishimoto et al (US Patent No. 5,888,510) in view of Raynauld et al. (2003).

Kishimoto et al. teach a method for inhibiting synovial cell growth by administering to a patient polyclonal or monoclonal antibodies to IL-6 or IL-6 receptor (see claims 1-4) and also teach a method of treating chronic rheumatoid arthritis by administering to a patient IL-6 antagonists including polyclonal or monoclonal antibodies to the IL-6 receptor (see claims 1-11; Example 2, columns 13-14). Kishimoto also teaches that IL-6 antibody binds to IL-6 and inhibits the binding between IL-6 and the IL-6 receptor and thus blocks IL-6 signal transduction, inhibiting inflammation which is IL-6 biological activity (see column 3, lines 53-60). Therefore,

Kishimoto discloses that if a cytokine causes a disease, an antibody to the cytokine will block the signal transduction by the cytokine, inhibit the cytokines biological activity and has an alleviating and therapeutic effect on the symptoms of the disease (see column 3, lines 41-52). However, Kishimoto does not disclose a method of treating osteoarthritis by administering an IL-6 antibody.

Raynauld et al teach that repeated injections of steroid to the knee of osteoarthritic patients is clinically effective for relief of symptoms of osteoarthritis (see abstract, column 2, last 8 lines; page 372, Table 1; page 373, Table 2). Raynauld et al. do not disclose a method of administering to a patient IL-6 antibodies to treat osteoarthritis.

Therefore, it would have been *prima facie* obvious to one having ordinary skill in the art, from the method of Kishimoto to administer IL-6 antibodies to patients together with corticosteroids for the treatment of osteoarthritis as taught by Raynauld et al to obtain the known functions and advantages thereof as per the teachings of both Raynauld et al and Kishimoto et al. Therefore, to substitute the medical agent, IL-6 antibodies, of Kishimoto et al., in the treatment of osteoarthritis together with administration of corticosteroids as shown by the teachings of Raynauld et al., would be obvious because both agents are used for the treatment of IL-6 induced inflammation. Claim 1, line 1, recites the open language "comprising administering" which encompasses administering multiple medical agents. One would have been motivated to administer IL-6 antibodies and corticosteroids to a patient because Kishimoto et al teach the properties of IL-6 antibodies and Raynauld et al provides the motivation to administer corticosteroids to inhibit the inflammation caused by IL-6. Therefore, treatment with these multiple agents would be expected to relieve the symptoms of osteoarthritis. Administration of both these agents would be effective

therapy for osteoarthritis because both these agents work to reduce inflammation caused by IL-6 in patient populations and corticosteroids work in both types of patients with rheumatoid arthritis and osteoarthritis to reduce inflammation caused by IL-6. Therefore, the teachings of both Kishimoto and Raynauld translate into a benefit for administering IL-6 antibodies and corticosteroids for treating patients with osteoarthritis.

6b. Claim 7 is rejected under 35 U.S.C. 103(a) as being unpatentable over Kishimoto et al. (US Patent No. 5,888,510) in view of Raynauld et al. (2003) as applied to claims 1-2, 6, 9-13, above, and further in view in of Queen et al. (U.S. Patent No. 5,530,101).

The disclosures of Kishimoto et al and Raynauld et al have been set forth above (see paragraph 6a above). However, neither Kishimoto et al nor Raynauld et al disclose a method of administering anti-human IL-6 antibodies for treatment of osteoarthritis.

Queen et al., (column 13, lines 5-65) teaches the humanization of monoclonal antibodies, as well as the issues involved in designing a humanized antibody that retains high affinity for its antigen. Queen et al., (column 17, lines 31-43) further teaches the production of antibody fragments, including the Fab fragment.

Therefore, at the time the invention was made, it would have been prima facie obvious to a person of ordinary skill in the art to administer as taught by Queen et al, humanized monoclonal antibodies to IL- 6 for treatment of osteoarthritis in a patient in a method as taught by Kishimoto in view of Raynauld et al. The motivation for doing so would have been the decreased immunogenicity of humanized antibodies when injected into humans, while the humanized antibodies retain their affinity for their epitope (Queen et al., (column 2, lines 5-8)).

Conclusion

No claim is allowed.

Claims 1-2, 6-13 are rejected.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Prema Mertz whose telephone number is (571) 272-0876. The examiner can normally be reached on Monday-Friday from 7:00AM to 3:30PM (Eastern time).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Nickol, can be reached on (571) 272-0835.

Official papers filed by fax should be directed to (571) 273-8300. Faxed draft or informal communications with the examiner should be directed to (571) 273-0876.

Information regarding the status of an application may be obtained from the Patent application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Prema Mertz/
Prema Mertz, Ph.D., J.D.
Primary Examiner
Art Unit 1646

